2/24/01

Office Action Summary	Application No. 08/591,651	Applicant(s) Classen
	Examiner Brenda Brumback	Group Art Unit 1642

☒ Responsive to communication(s) filed on *Dec 19, 2000* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *5, 6, 8, 10, 11, 15, 16, 19, 27-30, 32-41, 43, 44, 46, 48-52, 55-57, and 59-143* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *5, 6, 8, 10, 11, 15, 16, 19, 27-30, 32-41, 43, 44, 46, 48-52, 55-57, and 59-143* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. This action is responsive to the amendment filed 12/19/2001 with attachments. Claims 59, 64, 96, and 97 were amended. Claims 15, 26, 48, and 58 were canceled.

Claims 106-140, which were added by the amendment of 12/19/200, have been renumbered as 109-143 , according to 37 CFR 1.126 (see MPEP 608.01[j]).

Pending claims are 5, 6, 8, 10, 11, 16, 19, 27-30, 32-41, 43, 44, 46, 49-52, 55-57 and 59-143. Claims 6, 32, 33, 56-57, 101, 103, 106, and 128-143 are drawn to methods; claims 5, 8, 10, 11, 16, 27-30, 34-41, 43, 44, 46, 49-52, 55, 59-100, 102, 104, 105, and 107-127 are drawn to kits. Claim 19 is drawn to an immunogenic agent.

It is noted that claims 102-106 were inadvertently not considered in the previous Office action. These claims will be addressed herein.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

2. The information disclosure statement filed 02/01/2001 has been entered as Paper # 27. Note: Reference DK was not considered as no copy of the document was submitted; reference HM was not considered, as the document is in French and the IDS does not include a concise explanation of its relevance; references HU and HV were not considered, as no publication dates were provided; and reference IC was not considered, as only a title and no text was submitted.

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Claim Objections

3. The objections to claim 35 for a misspelling and to claim 37 for an informality in grammar are withdrawn pursuant to applicant's amendment thereof. The objection to claims 5, 6, 19, 30, 32, 56-58, 67, 69-71, 73, and 75- 77 for informalities in punctuation and nomenclature is maintained. While certain of the punctuation errors have been corrected, others have not. See for example claim 70, line 3. There should be a comma between "diphtheria" and "pertussis".

Applicant's arguments regarding the nomenclature have been fully considered but they are not persuasive. Applicant argues that when a disease name is recited, it is applicant's deliberate intent to cover any immunogen of any etiologic agent which causes that disease. Applicant's claims, however, do not recite "plaque" immunogen, for example. They simply recite "plague". "Plague" is the name of a disease, not an immunogen. The metes and bounds of the claimed immunogen(s) simply cannot be determined if the claim fails to recite it (them). Similarly, "pertussis" is the name of a disease, not an etiologic agent and "varicella" is the name of a disease, not an immunogen.

Claim Rejections - 35 USC § 112

4. The rejection of claim 77 under 35 U.S.C. 112, second paragraph, as being of improper Markush format is withdrawn due to applicant's amendment thereof. Claim 48 has been canceled.

The rejection of claims 5, 6, 8-11, 16, 19, 27-30, 34-57, 77, and 86 under 35 U.S.C. 112,

second paragraph, is maintained. Applicant's arguments have been fully considered but they are not persuasive.

Applicant argues that application of the rule of dependency for claims 11 and 38 in the present case is frivolous. The examiner does not agree. Because the antecedent basis of claims 11 and 38 is not clear, the metes and bounds of the claimed invention cannot be determined.

Regarding applicant's argument in the Brief that substantially has been repeatedly upheld when a suitable standard is disclosed, the examiner maintains that no such standard has been established in the present case. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Applicant's argument that the law does not require that a range be fixed with a lower limit is not persuasive absent some identification of the particular law or laws to which applicant is referring. Absent a recitation of a lower limit, the metes and bounds of the claimed range cannot be determined and the claim is indefinite.

Applicant argues that defining an immunogen by the associated disease is broader than defining the etiologic agent but is not indefinite. However, the immunogens of the instant claims are in the form of a Markush group. The members set forth in a Markush group must belong to a recognized physical or chemical class or to an art-recognized class (MPEP 2173.05(h)). In the instant case, the members of the recited Markush groups are not members of a recognized class and do not have a common property which relates them. A disease is unrelated in structure and

function to an immunogen. Furthermore, recitation of a disease name does not define the metes and bounds of an immunogen. Applicant's argument that a person skilled in the art can readily determine whether an immunogen is associated with a particular disease is noted; however, absent sufficient teaching of which immunogens that are associated with a particular disease are encompassed within the claimed invention, the metes and bounds of the invention cannot be ascertained and the claims are indefinite.

Regarding the term "herpes", recitation of this term without defining which of the myriad of herpesviruses are encompassed within the claimed invention is indefinite. One of skill in the art simply would not be apprised of the metes and bounds of the immunogens encompassed.

Applicant's argument that a cross-reactive molecule is not required to elicit a protective immune response is noted; however, it is unclear how this is germane to the present rejection of claim 19 for the phrase "a molecule that cross reacts immunologically to at least one of said immunogens". The claim is indefinite because the specification fails to teach the metes and bounds of such a molecule having immunological cross reactivity; it is not based on elicitation of any immune response.

Applicant's arguments pertaining to claim 48 are moot, as claim 48 has been canceled.

5. The rejection of claims 5, 6, 8-11, 16, 30, 32, 38, 49, 55-57, and 59-65, 72, 74-101 under 35 U.S.C. 112, first paragraph, for new matter rejection is maintained.

Applicant's response does not include additional arguments pertaining to the "where, if only one immunogen is administered according to said immunization schedule, that immunogen is one other than BCG" and "if said one immunogen is whole cell pertussis, the schedule is one other than a schedule of three doses at one week intervals, all given in the first month" language found in claims 32 and 56. Regarding the arguments in section 7 of the Brief, as was set forth in the previous Office action, matter not in the originally presented specification, claims, or drawings of the present application, is considered to be new matter (see MPEP 608.04(a)). Applicant cannot rely upon an issued patent from a parent case or upon cited literature, rather than the present specification, to provide support for amendments to the claims in the present application.

Regarding claim 59 and the label warning, the examiner finds no reference at all to warning labeling or instructions at pages 51-52; at page 7, lines 11-14; or at page 54, lines 14-21. The references sections are general discussions of kits , the lack of warnings on package inserts, and screening trial. None of the referenced sections, either singly or in combination, provide support for applicant's claim limitations. One simply would not envision the claimed specific warning instructions from reading the referenced portions of the disclosure.

While the section of the disclosure referenced by applicant at page 75, line 13-17, does teach using a non-living vaccine lacking an aluminum-based adjuvant, it does not provide support for excluding "another adjuvant whose ability to activate macrophage is about the same as or greater than that of an aluminum salt".

6. The rejection of claims 5, 6, 8, 10, 11, 16, 19, 27-30, 32-41, 43, 44, 46, 49-52, and 55-57, and 58-101 under 35 U.S.C. 112, first paragraph is maintained. Claims 103, 106, and 128-143 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant's arguments and enclosures have been fully considered but they are not persuasive for the following reasons.

Applicant's arguments and exhibits allege that there was a bias on the part of the director of the Institute for Vaccine Safety (Dr. Neal Halsey) and that this bias was reflected in the PIDJ article. Applicant cites Exhibits A2 and E2 in support of this allegation. Exhibits A2 and E2 would seem to be primarily related to an alleged lack of consensus regarding a contributory role for immunizations in the development of type 1 diabetes mellitus and an alleged bias on the part of Dr, Halsey in favor of vaccinations; it does not seem to be related at all to the claimed methods for reducing the incidence or severity of diabetes or other chronic immune-mediated disorder through immunization. Therefore, the relevance of this argument and the exhibits to the present rejection is not readily apparent. Nevertheless, applicant's argument that the teachings of the PIDJ are a result of conflict of interest, rather than scientific evidence, do not seem to be supported by the general teachings of the art. See, for example, DeStafano et al. (reference DU), EURODIAB Substudy 2 Study Group (reference EB), Graves et al. (reference EF), Heijbel, et al. (reference EI), Hiltunen et al. (reference EL), Jefferson et al. (reference EQ), Karvonen et al.

(reference EV), Bedford H. (reference HD), Petousis-Harris et al. (reference HE), Dahlquist et al. (reference HK), Jefferson T.O. (reference HP), Elliott et al. (reference IJ), and Anonymous (reference IN), all of record in the IDS filed 02/01/2001 (Paper # 27), and all of which teach that there is no apparent association of any schedule of dosing of any known immunizations, either contributing to or reducing the incidence or severity, with type 1 diabetes mellitus.

Applicant's arguments drawn to utility guidelines are not germane to the present rejection, which has been made under 35 U.S.C. 112, first paragraph, as lacking sufficient disclosure to enable one of skill in the art to make and use the claimed invention. There has been no utility rejection made to date over the pending claims.

Regarding the data presented in the disclosure referenced by applicant in support of the claimed association between immunization and onset and/or severity of diabetes and other immune-mediated diseases, this data is not conclusive of a causal relationship because it is epidemiological. It is well known in the art that epidemiological data may be used to generate hypotheses regarding possible factors associated with a particular disease; however, epidemiological data alone does not establish a causal relationship (see PIDJ, page 219, the sentence bridging columns 1 and 2).

Applicant argues that "Applicants have shown that in a recognized animal model of SLE, early immunization reduces the incidence of SLE (Example 5)". However, in the present case, the extrapolation of data based on a mouse model to humans and other mammals is questionable because of the criticality of the age of administration of the immunogen and the differences in

maturation rates between rodents and humans. Elliott et al. (reference IJ) teaches that in the case of extrapolation of data from the NOD mouse to the initiation of islet autoimmunity in humans, "Great caution should be exerted in extrapolating results from the NOD mouse to humans, as the time scales for effective prevention are so different" (see the last sentence of the abstract). Because of the absolute criticality of the age of administration of the immunogen in the claimed methods, and in light of the teachings of unpredictability in the art, there would not be a reasonable expectation of success in humans based on data from a mouse or rat model.

Regarding applicant's argument that there are now a large number of reports indicating vaccines may cause chronic immune mediated disorders, exhibits 1E, 5G, 1A, 5H, 5E, and Classen references, applicant is reminded that the present methods are drawn to reducing the incidence or severity of chronic immune-mediated disorders, not the converse. Thus, the relevance of this line of argument is not apparent.

Claim Rejections - 35 USC § 101/ Double Patenting

7. The rejection of claims 2-14, 16-17, 19, 21, 23-25, 27-33, 34-47, 49-55, 56-57, and 101 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-42 of Classen U.S. Patent No. 5,728,385 and claims 1-47 of Classen U.S. Patent No. 5,723,283 is maintained. Applicant's intent to file a terminal disclaimer upon indication of allowable subject matter is noted.

8. Claims 102-143 are also rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-42 of Classen U.S. Patent No. 5,728,385 and claims 1-47 or Classen U.S. Patent No. 5,723,283 for the reasons of record.

Claim Rejections - 35 USC § 102

9. The rejection of claims 8, 10, 11, 16, 19, 27-30, 34-41, 43, 44, 46, 49-52, 55, 59-67, 72, 73, 76-77, 79, 89, 90, 92, 9, and 96-100 under 34 U.S.C. 102(b) as being anticipated by Madore et al. (of record in Paper # 7) is maintained. Claims 102, 104, 105, and 107-127 are also rejected under 34 U.S.C. 102(b) as being anticipated by Madore et al. for the reasons of record.

10. The rejection of claims 5, 6, 8, 10, 11, 16, 19, 27-30, 32-41, 43, 44, 46-47, 49-52, 59-67, 70-73, 76, 78, 79, 90, 92, 93, 96-100 under 35 U.S.C. 102(b) as anticipated by Dengrove et al. (of record in paper # 7) is maintained. Claims 102, 104, 105, and 107-127 are also rejected under 35 U.S.C. 102(b) as being anticipated by Dengrove et al. for the reasons of record.

11. The rejection of claims 5, 6, 8, 10, 11, 16, 19, 27-30, 32-41, 43, 44, 46-47, 49-52, 59-67, 70-73, 76, 78, 79, 90-93, and 96-100 under 35 U.S.C. 102(b) as anticipated by Halsey et al. (of record in paper # 7) is maintained. Claims 102, 104, 105, and 107-127 are also rejected under 35 U.S.C. 102(b) as anticipated by Halsey et al. for the reasons of record.

12. The rejection of claims 5, 6, 8, 10, 11, 16, 19, 27-30, 32-41, 43, 44, 46-47, 49-52, 60-67, 70, 72, 73, 78, 79, 90, 91, and 96-100 under 35 U.S.C. 102(b) as anticipated by John is maintained. New claims 102, 104, 105, and 107-127 are also rejected under 35 U.S.C. 102(b) as anticipated by John for the reasons of record.

13. The rejection of claims 5, 8, 10, 11, 16, 19, 27-30, 34-41, 43, 44, 46, 49-52, 55, and 59-100 under 35 U.S.C. 102(b) as being anticipated by Benveniste and Lagrange et al., is maintained. New claims 102, 104, 105, and 107-127 are also rejected under 35 U.S.C. 102(b) as anticipated by Benveniste and Lagrange et al. for the reasons of record.

14. Applicant's argument set forth in section 5.1 of the Brief that there is a functional relationship between the printed matter or labeling in the claimed kits and the immunogens have been fully considered and previously addressed. To reiterate, they are not persuasive because applicant has not demonstrated the existence of any such functional relationship. The immunogens of the claimed kits remain functional absent the labeling; therefore no functional relationship exists between the labeling and the immunogens that would be given patentable weight. In re Miller and In re Gulak relate to a mathematical device and to a measuring cup respectively. In each of these cases, the function of the device depends upon the printed matter itself which is a part of the substrate; without the printed indicia or numbers, the substrates lose

their function. Such is not the case with the instant kits. The immunogens remain fully functional absent the labeling or printed instructions for use.

Regarding applicant's arguments that the PTO has allowed claims with labeling limitations previously, such arguments are not persuasive because it is not clear how patents to such inventions as a drug dosage identification card, a drinking vessel, and a prescription drug package are relevant to the present rejection. Furthermore, it is well settled that whether such claims have been allowed to others is immaterial. In re Giolito, 530 F.2d 397, 188 USPQ 645 (1976).

Conclusion

15. Due to the new grounds of rejection herein, this action is made nonfinal.

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Anthony Caputa whose telephone number is (703) 308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1642 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1642 FAX telephone number is (703)-305-3014. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a

Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

BB
February 20, 2001

Brenda Brumback
Brenda Brumback,
Patent Examiner